

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference PC04010LGLS | FOR FURTHER ACTION See Form PCT/IPEA/416 | |
| International application No. PCT/KR2004/002139 | International filing date(day/month/year) 26 AUGUST 2004 (26.08.2004) | Priority date (day/month/year) 27 AUGUST 2003 (27.08.2003) |
| International Patent Classification (IPC) or national classification and IPC IPC7 C07D 261/04 | | |
| Applicant LG LIFE SCIENCES LTD. et al | | |

- This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, comprising:
 - ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____ containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

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| Date of submission of the demand 22 MARCH 2005 (22.03.2005) | Date of completion of this report 28 JUNE 2005 (28.06.2005) |
| Name and mailing address of the IPEA/KR  Korean Intellectual Property Office 920 Dunsan-dong, Seo-gu, Daejeon 302-701, Republic of Korea Facsimile No. 82-42-472-7140 | Authorized officer Yoon, Kyung Ae Telephone No. 82-42-481-5605  |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/KR2004/002139

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
 - ☒ the international application as originally filed/furnished

 - ☐ the description:
 - pages _____ as originally filed/furnished
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the claims:
 - pages _____ as originally filed/furnished
 - pages* _____ as amended (together with any statement) under Article 19
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the drawings:
 - pages _____ as originally filed/furnished
 - pages* _____ received by this Authority on _____
 - pages* _____ received by this Authority on _____

 - ☐ the sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages _____
 - ☐ the claims, Nos. _____
 - ☐ the drawings, sheets _____
 - ☐ the sequence listing (*specify*): _____
 - ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages _____
 - ☐ the claims, Nos. _____
 - ☐ the drawings, sheets _____
 - ☐ the sequence listing (*specify*): _____
 - ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/KR2004/002139

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

| | | | |
|-------------------------------|--------|--------|-----|
| Novelty (N) | Claims | 1-21 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 1-21 | YES |
| | Claims | | NO |
| Industrial applicability (IA) | Claims | 1-19 | YES |
| | Claims | 20, 21 | NO |

2. Citations and explanations (Rule 70.7)

The following documents are referred to in this report:

D1: KR 1999-0079268 A (05 Nov. 1999)

D2: WO 01/21600 A1 (29 March 2001)

D3: WO 95/14681 A1 (01 June 1995)

D4: WO 95/14680 A1 (01 June 1995)

D5: WO 94/12481 A1 (09 June 1994)

1. Novelty

The subject-matter of claims 1-21 in the present invention relates to an isoxazoline derivative of formula (1) as an inhibitor against various caspases, a process for preparing the same, and a therapeutic composition for preventing inflammation and apoptosis comprising the same.

D1 discloses an isoxazoline derivative as an inhibitor against interleukin-1 β converting enzyme(ICE or caspase 1) and apopain/CPP-32(caspase 3). D2 discloses isoxazoline derivatives as a caspase inhibitor and they can be effectively used in treating diseases due to caspases such as dementia, cerebral stroke, AIDS, diabetes, gastric ulcer, hepatitis, sepsis, organ transplantation rejection, and inflammation. D3 and D4 disclose isoxazoline derivatives which are selective inhibitors of phosphodiesterase type IV and they are useful as anti-inflammatory agents. D5 discloses isoxazoline derivatives having the ability to inhibit a 5-lipoxygenase enzyme and they are useful as anti-inflammatory agents.

None of D1-D5 discloses the isoxazoline derivative of formula (1) in the present invention.

Therefore, claims 1-21 of the present invention can be considered to be novel over D1-D5[Article 33(2) PCT].

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

Box V.

The both isoxazoline derivatives in D2 and the present invention have the same backbone structures, but slightly different substituents. According to the comparison data (Table 5) of experiment 7 written in the specification of the present invention, the compound of formula (1) in the present invention is surprisingly superior to the isoxazoline derivative (LB84068MP) in D2 in terms of the inhibitory effect against caspases and the solubility.

Therefore, the inventive step of claims 1-21 can be acknowledged over D2 [Article 33(3) PCT].

3. Industrial Applicability

The subject-matter of claims 1-19 appears to be industrially applicable.

The subject-matter of claims 20 and 21 relates to a method of therapeutic treatment and a medical use of the formula (1) compound. Concerning the assessment of the industrial applicability of the subject-matter relating to therapeutic applications, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claim [Article 33(4) PCT].